June 8, 1947.

Dr. J. Monod,
Service de Microbiologie,
Institut Pasteur,
Paris, France.

Dear Jacques:

This letter is inspired by the publication (at last) of the Cold Spring Harbor Symposium of last summer, which has given me an opportunity to refresh my memory concerning certain details discussed by Prof. Lwoff, and I think entre nous on the sand of CSH. They concern the interaction of the galactose -/+ and lactose -/+ mutations, in particular whether they concern allelic changes at the same locus, or interactions of distinct genes.

We discussed, last summer, the possibility of a direct attack on this problem, with recombinational techniques, using mutant strains of K-12. You pointed out at that time, however, that it would be necessary to have a mutabile, or at least, a pair of related Lac- and Lac+ strains. I should like to let you know now that I have such strains and have been using them for some time as convenient genetic markers in linkage studies. Lac- mutants in previously established multiple biochemical mutant stocks were looked for after treatment with uv and nitrogen mustard by plating cells on lactose-EMB agar, and looking for white colonies. Two have been found, out of about 5×10^4 colonies examined. One of these (in a threonine-leucine-thiamin-less stock)(Y53) is typically mutabile and not infrequently throws off Lac+ papillae ; the other, (in a biotin-methionine-less, T1-resistant stock)(Y87) is likewise Lac- but to my knowledge does not revert to Lac+. These mutants are characterized by their ability to produce acid from lactose on EMB plates; I have not studied them in synthetic medium in any detail.

I am planning to use these stocks for studies on mutation (there seems, for example, to be a genetic differential between them) and for the examination of the possibility of physiological differences between independent reversion stocks (in hopes of finding multiple alleles) but I should be delighted to send them to you if you would care to use them in relation to this problem. Assuming that these and other stocks are 'galactose -', for eaxmple, you could cross a B-M-G-Lac+ with a T-L-B_1-G+Lac- to determine whether, in the prototrophs, there were any recombinations, of the type G+L+ or G-L-.

I think you should have no difficulty in performing such crosses according to the techniques that have been or are about to be published; if you would prefer it, I would be willing to isolate a series of prototroph recombinants and send them to you for testing. The preliminary work and the determination of the growth rates however is just a bit out of my milieu, and I haven't the time for it.

Dave Bonner tells me you are expected in the States this summer. Probably I shan't be here then, but at Woods Hole; drop up if you have a chance, particularly if you are interested in these propositions. Anyhow let me know whether to send along the cultures.

Please extend to Prof. Lwoff most sincere regards from Dr. Tatum and myself; we look forawrd to seeing you again.

Yours sincerely,

Joshua lederberg.

P.S. [illegible]